## REMARKS

**Status of Claims and Amendment**

Claims 1, 3, 4, 12, 13, and 18 are amended. Claims 2, 6-11, 17, 19, and 20 have been canceled. Claims 6-10 and 21-27 are withdrawn as being directed to a non-elected invention. Claims 1, 3, 4, 5, 12-16, and 18 are all the pending claims being examined in the present application. Claims 1-5 and 11-20 are rejected.

Claim 1 has been amended to incorporate the limitations of claim 2, and to include the recitation "the acyl group receptor is selected from the group consisting of hydroxyl alkanoate CoA (HA CoA) and poly(hydroxyl alkanoate) (PHA-CoA)" Support for the amendments to claim 1 may at least be found at page 22, line 27 to page 29, line 28 of the specification.

Claims 3, 4, 12, and 13 have been amended to depend from claim 1. In addition, claim 13 is amended to replace "acyl thioester" with "acyl ester of a thiol compound." Support for the amendment to claim 13 may be found at least at page 14, line 19 of the specification.

Claim 18 has been amended to be dependent on claim 1, and to recite the process for preparing polyhydroxy alkanoate synthase derived from *Ralstonia*. Support for the amendment to claim 18 may at least be found at the paragraph bridging pages 43-44 (Referential Example 4) of the specification.

**Claim of Priority**

Applicants thank the Examiner for acknowledging Applicants' claim of priority to Japanese Application No. 2003-13762 filed January 22, 200, and Japanese Application No. 2003-94881 filed March 31, 2003, as well as receipt of the certified copies of the priority documents.

**Information Disclosure Statement**

Applicants thank the Examiner for acknowledging the Information Disclosure Statement filed July 20, 2005, and for returning a signed and initialed copy of the PTO/SB08 form submitted therewith.

**Restriction Requirement/Election of Species**

Applicants thank the Examiner for acknowledging Applicants' election of Group I (claims 1-20) without traverse and the Election of Species without traverse filed September 4, 2007, and October 12, 2007.

**Response To Rejections Under 35 U.S.C. §112, first paragraph**

**A.** Claims 1-5 and 11-20 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description and enablement requirements.

According to the Office Action, the claimed "acyl group receptor" is not enabled by the specification because paragraph [0078] of the present specification (see Published Application No. US 2006/0148048 A1) instructs that the acyl group receptor may be selected without particular limitation and includes substances which are not usually an appropriate substrate for the enzyme.

In response, Applicants note that one of ordinary skill in the art would understand from reading the specification, that because an acyl group receptor may be used as a substrate for the CoA enzyme of an acyl transfer reaction, the hydroxyl alkanoate and poly(hydroxyl alkanoate may be used a substrate for a CoA enzyme, as described by the polymer-producing reaction at page 22, line 27 to page 29, line 28 of the specification. Also, as shown in the formula at page 27 of the specification, (P)HA-CoA having the repetition number, n, receives an acyl group from

acyl coenzyme A (HA CoA) to add 1 to n, so that PHA-CoA having the repetition number n+1 can be generated, and is an acyl group receptor.

Thus, based upon the disclosure in the present specification, one of ordinary skill in the art possessing common technical knowledge and common technical sense would be able to select an acyl group receptor from the group consisting of hydroxyl alkanoate CoA and poly(hydroxyl alkanoate) CoA, and practice the claimed invention without undue experimentation.

Further to advance prosecution, claim 1 has been amended to recite that the claimed acyl group receptor is selected from the group consisting of hydroxyl alkanoate CoA (HA-CoA) and poly(hydroxyl alkanoate) (PHA-CoA).

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

**B.** Claims 18- 20 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Office Action requires the structure of the specific enzyme claimed or a deposit for E. coli pQEREC (E. coli incorporating the pQEREC plasmid) so as to enable preparation of the synthase of claim 18. Alternatively, the Office Action suggests that the rejection may be overcome by amending claim 18 to a product-by-process format.

In response, claim 18 has been amended to product-by-process format, i.e., to recite a method by which the claimed polyhydroxy alkanoate synthase derived from genus *Ralstonia* is prepared, as suggested by the Office Action.

Claims 19 and 20 are canceled. Thus, the rejection with regard to claims 19 and 20 is rendered moot.

Accordingly, withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

**C.** Claims 1-5 and 10-20 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Office Action asserts that although the specification is enabling for the specific strain E. coli B21 (pQEREC), the specification does not enable other synthases.

Applicants respectfully disagree. As shown below one of ordinary skill in the art would be enabled, based upon the guidance provided in the specification, and common technical knowledge of the common recombinant techniques well-known to those of ordinary skill in the art, how to make the presently claimed polyhydroxy alkanoate synthase without undue experimentation.

For example, one of ordinary skill in the art would understand from reading the specification at Referential Example 4 (page 43-44) and page 25, line 9 to page 26, line 7, that the polyhydroxy alkanoate (PHA) synthase derived from *Ralstonia eutropha* ATCC 17699, and purified following high enzyme expression in *E.Coli* B21 (pQEREC), as described in the specification, may be carried out for other synthases derived from other sources of living organisms such as, genus *Ralstonia*, genus *Pseudomonas*, genus *Chromatium*, genus *Ectothiorhodospira* (see paragraph bridging pages 25-26 of the specification), using common recombinant techniques known in the art. Such disclosure in the specification is an example of preparing the presently claimed PHA synthase using a common technique that is well-known to one of ordinary skill in the art to make and purify high copies of a desired protein. Further, as described by Antonio et al., Analysis of in-vivo substrate specificity for the PHA synthase from Ralstonia cutropha: formation of novel copolyesters in recombinant Escherichia coli, FEMS

Microbiology Letters 182(1): 111-117 (2000)[1] ("Antonio"), polyhydroxy alkanoate synthases derived from *Ralstonia eutropha* and *Allochromatium vinosum* may be generated using recombinant E.Coli.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

**Response To Rejections Under 35 U.S.C. § 112, second paragraph**

Claims 1-5 and 11-20 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite with respect to the scope of the claimed "acyl group receptor", namely, that there is no limitation as to use as a substrate for the claimed CoA enzyme.

In response, Applicants believe that the claims prior to the present amendment clearly define what Applicants consider to be their claimed invention. However, to advance prosecution, claim 1 has been amended to recite that the acyl group receptor is selected from the group consisting of hydroxyl alkanoate CoA (HA-CoA) and poly(hydroxyl alkanoate) (PHA-CoA).

Claims 3, 4, and 18 have been amended to depend on claim 1.

Claims 2, 11, 17, 19, and 20 have been canceled. Thus, the rejection with regard to claims 2, 11, 19, and 20 is rendered moot.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

[1] Submitted in the Information Disclosure Statement filed July 13, 2006.

**Response To Rejections Under 35 U.S.C. § 102**

Claim 1-3 were rejected under 35 U.S.C. §102(b) as being by Ouyang et al. (J. Organic Chemistry 56(11): 3752-3755 (1991); "Ouyang"). Ouyang (which is aid to teach a general reaction for reproducing acyl coenzyme A) was cited as meeting each of the terms of the rejected claims.

Applicants respectfully traverse.

Ouyang does not explicitly or inherently disclose the presently claimed method for at least the following reasons.

Ouyang discloses a "new chemical method for preparing some unnatural CoA thioesters in aqueous buffer systems and for recycling acetyl-CoA thioesters in enzyme-catalyzed reactions" (see page 3753, 1st column, 2nd full paragraph of Ouyang). Ouyang is different from the presently claimed method because although the reaction of Ouyang involves a thioester exchange, the reaction uses S-acetylthiocholine to recycle CoA (see page 3753, Scheme II and 2nd column, 1st sentence of 1st full paragraph of Ouyang) and citrate synthase to catalyze the reaction (see page 3754, 1st column, 4th sentence of 1st full paragraph of Ouyang).

In contrast, the presently claimed invention requires the combination of a thioester exchange reaction and a macromolecular polymerization reaction, as disclosed at page 27 of the specification. The presently claimed reaction uses the claimed hydroxyl alkanoate CoA (HA CoA) or poly(hydroxyl alkanoate) (PHA-CoA) as substrates for the CoA enzyme and an acyl group is added to the HA CoA or PHA-CoA. Further, as acknowledged at page 7 of the Office Action, Ouyang does not disclose the presently claimed enzymes. In particular, Ouyang does not disclose the presently claimed polyhydroxy alkanoate synthase.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b), second paragraph, is respectfully requested.

**Response To Rejections Under 35 U.S.C. § 103(a)**

Claims 1-5 and 11-20 were rejected under 35 U.S.C. §103(a) as being unpatentable over Ouyang, Antonio, and Yuan et al. (Archives Biochem. Biophys. 394(1): 87-98 (2001); "Yuan"), each alone or in combination.

The Office Action acknowledged that the cited documents do not disclose the specific synthase disclosed in the present specification. The Office Action also acknowledged that the cited documents do not specifically disclose an aromatic thiol or a thiophenol.

The Examiner's position was that the cited documents "provide guidance for [one of skill in the art to]…[reproduce]…acylcoenzyme A with a thiol compound", and that the claimed reaction would be obvious (in view of the cited references which are said to employ other PHA synthases) to one of skill in the art possessing common technical knowledge, citing KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (2007).

Furthermore, in view of *KSR*, the Examiner disregards the "PCT action dated May 11, 2004[, which indicates] that claims 4-5 and 13-16 [are] considered novel and patentable over the art of record." (See page 8, 1st sentence of 1st full paragraph of the Office Action).

In response, Applicants note that to establish a *prima facie* case of obviousness, "the prior art reference (or references when combined) must teach or suggest all the claim limitations." M.P.E.P. §2143. *KSR* did not change this fundamental requirement. Because Ouyang does not disclose the presently claimed method for at least the reasons discussed above, i.e., Ouyang does not disclose a macromolecular polymerization reaction nor polyhydroxy alkanoate synthase, Ouyang fails to render obvious the presently claimed method.

In addition to the arguments discussed above, the Office Action has acknowledged that the cited documents do not disclose the claimed "synthase" (claim 17) nor the claimed aromatic thiol (claim 4) or a thiophenol (claim 5).

Further, and for at least the following reasons, the Office Action fails to provide "some suggestion of the desirability of doing what the [present inventors] have done…[to] support the conclusion that the claimed invention is directed to obvious subject matter" because there is nothing in the "prior art as a whole to suggest the *desirability*, and thus the obviousness, of [combining]" the teachings of Ouyang, Antonio, and Yuan. M.P.E.P. §2143 and §2143.01.

Antonio does not cure the deficiencies of Ouyang. Although Antonio discloses polyhydroxyalkanoate (PHA) synthase derived from *Ralston eutropha*, Antonio is directed to investigating the "in vivo substrate specificity of the type I polyhydroxyalkanoate (PHA) synthase from *Ralston eutropha*" [emphasis added] (see Abstract of Antonio). In addition, even though Antonio teaches acetyl donors from SCHEMES II to V, Antonio does not teach or suggest recycling CoA. Accordingly, one of ordinary skill in the art would not have been motivated to combine Antonio and Ouyang for at least these reasons.

However, even if Antonio was combined to modify Ouyang with regard to the use of polyhydroxyalkanoate (PHA) synthase, the combination of Antonio and Ouyang would not result in the presently claimed method which requires the combination of a thioester exchange reaction and a macromolecular polymerization reaction.

Further, even if one of ordinary skill in the art of polymerization had been aware of the techniqued disclosed in Ouyang, which does not concern polymer synthesis, one of ordinary skill in the art would not have been motivated to combine the method of Ouyang with polymer synthesis. Since PHA polymerization is characterized by continuous reactions of polymers

where a compound generated in one reaction may serve as a substrate in the subsequent reaction, the technical field of the presently claimed method is in a different category from the enzymatic reaction to produce citric acid with citrate synthase disclosed in Ouyang.

Similarly, Yuan adds nothing further to the teachings of Antonio because Yuan is also directed to characterizing the substrate specificity of class I and III polyhydroxyalkanoate (PHA) synthase from *Ralston eutropha*. (See Abstract of Yuan). Further, Yuan appears to disclose that "*[i]n vitro* results differ from studies *in vivo*" for the substrate specificities of the PHA synthases (see last sentence of Abstract and page 96, paragraph bridging 1st and 2nd column of Yuan).

One of ordinary skill in the art would not have been motivated to combine the Ouyang, Antonio, and Yuan. Even if one of ordinary skill in the art should combine these documents, the resulting technique would be different from the claimed method which provides *in vitro* polymerization.

Claims 2, 11, 19, and 20 have been canceled. Thus, the rejection with regard to claims 2, 11, 19, and 20 is rendered moot.

**Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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